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What About the Environment?: Exploring the Neglected Third Dimension of Antimicrobial Resistance

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Abstract

Antimicrobial resistance (AMR) is one of the most urgent and complex health risks of our time, with links to human health, animal health, and the environment. The majority of research and policy related to AMR, however, has been dedicated to human and animal health. The third dimension — the environment — has been relatively neglected. Conversations about this problem have begun, but gaps in understanding remain. This study explores the key barriers that have hindered developments related to the environmental aspect of AMR and some of the solutions that have begun to or could be utilized to overcome these barriers.

A grounded theory approach was used to critically analyze qualitative data from expert interviews and field observations, quantitative data from the Global Database for Antimicrobial Resistance Country Self Assessment, and supplementary data from scientific and gray literature. While this study revealed many barriers — including characteristics of the issue like its complexity, gaps in research, conflict with existing norms and priorities, leadership failures, and country-level differences — just as many, if not more, solutions were identified. These included awareness-raising campaigns, emphasis of the links between AMR in the environment and other prominent issues like climate change to boost funding for research, increased surveillance, the introduction of policies to enhance coordination and collaboration among international agencies and national ministries, the inclusion of environmental leaders in the development and implementation of plans to combat AMR, and technical and financial support for developing countries. These and other solutions will be crucial not just to overcoming the neglect of the environmental aspect of AMR, but also to tackling this global health threat as a whole.

Key Words: global health, antimicrobial resistance, AMR, One Health, environment

Preface

The process of reading through the literature, pondering the issues and considering my own interests, and eventually settling upon a topic for my Independent Study Project (ISP) was rather lengthy and challenging. It taught me that good research takes time and a significant amount of effort and support. In trying to focus on one issue, I quickly realized that most of the global health challenges that we face in the twenty-first century are highly complex and extremely interconnected. Once I decided that I wanted to study something about which I knew relatively little prior to this semester — the environmental dimension of antimicrobial resistance (AMR) — I began to read everything that I could about this topic. As I dove deeper into scientific and gray literature, I found myself becoming familiar with terms, authors, concepts, and theories. I saw that this topic connected in one way or another to each and every one of my very broad interests, from climate change to agriculture, from development to public health. This experience was incredibly valuable for me as a person, as a student, and as an aspiring global health professional. I learned more than I ever could have imagined, in terms of both technical research skills and issue-specific knowledge. I found myself falling in love with the research process — something I was not sure that I enjoyed very much prior to this experience. I intend to build upon my ISP research in the future, and I am excited to see where this issue leads me next.

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I would also like to thank each of my interviewees: Dr. Sabiha Essack, Dr. Elizabeth Tayler, Dhafer Al Salah, Dr. Didier Wernli, Dr. Astrid Wester, and Mirza Alas. Each was incredibly helpful and went above and beyond to provide me with additional resources, connect me with fellow experts, and support me in any other way that he or she could. Finally, I am very grateful to the Stamps Foundation and to Tulane University for financially supporting my study abroad experience and enabling me to conduct this research project.

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1. Introduction

Antimicrobial resistance (AMR) — the ability of bacteria, parasites, viruses, and fungi to resist antibiotics, antivirals, and antimalarials (WHO, 2019d) — is "one of the most urgent health risks of our time," according to World Health Organization (WHO) Director-General Dr. Tedros Adhanom Ghebreyesus (WHO, 2019c). It was declared one of WHO's top 10 threats to global health in 2019 due to its massive scale and serious implications. In 2016, an estimated 700,000 deaths per year were attributed to infections by drug-resistant pathogens; this is expected to rise to 10 million by 2050 (Robinson et al., 2016). AMR also jeopardizes the achievement of the Sustainable Development Goals (SDGs), in particular Goal 3, which aims to promote wellbeing and ensure healthy lives for all (Lomazzi, Moore, Johnson, Balasegaram, & Borisch, 2019).

AMR poses a significant challenge to the global health community due to its complexity, which requires the involvement of many disciplines in finding effective solutions. Though "AMR occurs naturally over time…the misuse and overuse of antimicrobials is accelerating this progress" (WHO, 2018a, n.p.). This necessitates the input of the human health sector. The extensive use of antimicrobials in animal production practices both to preserve health and as growth promoters requires the additional contribution of the animal health sector in efforts to combat AMR (FAO, 2019). Beyond human and animal health, the environment is also involved. As a result of anthropogenic activities, "antimicrobial residues and antimicrobial resistant bacteria are found in surface waters, soils, animal and human waste streams, and foods of plant origin" (FAO, 2018, p. 1). The many factors at play across the human health, animal health, and environmental sectors (see Figure 1 on page 2 for a visual that conveys these factors and their complex interactions) have necessitated the use of a new approach for assessing and addressing this issue: One Health.

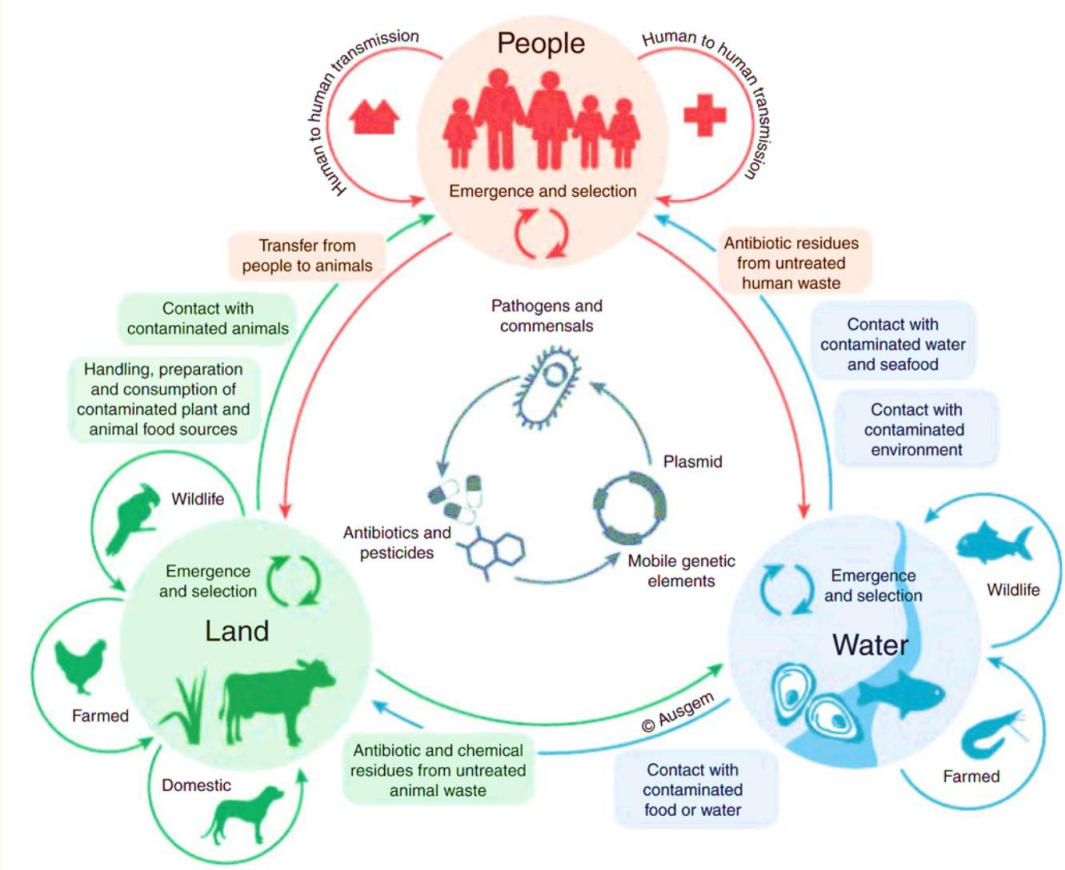

Figure 1. One Health system diagram showing the spread of AMR (Djordjevic & Morgan, 2019).

A One Health approach encourages collaboration and communication among disciplines across the human-animal-environmental interface (WHO, 2017b). It is defined as "the collaborative effort of multiple disciplines—working locally, nationally and globally—to attain optimal health of people, animals, and our environment" (AVMA, 2008, p. 13). One Health was developed in response to the realization that the fragmented framework historically utilized for health governance is not able to meet the complex health challenges of the 21st century (Queenan et al., 2017), a primary example of which is AMR. As such, WHO (2017) and others have recommended the application of a One Health approach to confront this global health threat.

Despite widespread agreement that AMR is the "quintessential One Health issue" (Robinson et al., 2016), relatively little attention has been given the environmental dimension of

this issue. Significant progress has been made in terms of research and policies pertaining to the other two dimensions — human health and animal health — but far less has been achieved on the environmental side. In fact, the environmental aspect of AMR has been referred to as "the neglected component of the One Health triad" (Essack, 2018b, p. e238). Explanations for gaps in research and policy at the global and national levels are few, and solutions are even fewer.

Thus, the purpose of this study is to explore the neglect of the environment in relation to AMR and to add nuance — in the form of expert perspectives and original analysis — to the emerging discussion about this issue. The two-part question that will be investigated is: Why has the environmental aspect of AMR been neglected and what can be done to prevent this neglect from occurring in the future? Two main research objectives were derived from this question:

⇒ **Obj. 1:** Identify and analyze the main barriers that have hindered research and policy developments related to the environmental aspect of AMR.

⇒ **Obj. 2:** Identify and analyze existing and potential solutions to overcome these barriers.

In this paper, the chosen methodology is first explained and justified. A review of scientific and gray literature follows, highlighting what is known about the topic and where gaps remain. The results are then presented and analyzed by thematic category in two main sections — barriers and solutions — that correspond to the two research objectives. Finally, evidence-based conclusions are drawn and recommendations for future research and policy are provided.

2. Research Methodology

An exploratory method was chosen for this study because of its usefulness in deriving explanations for poorly understood phenomena like the "neglect" of the environmental aspect of AMR. Data was primarily qualitative, but some quantitative data was also utilized. This mixed-methods approach allowed for a more thorough and complex analysis of the issue.

In terms of data collection, the investigation began with a broad review of literature about AMR to develop a foundational understanding of this complex issue and relevant scientific and governance-related progress. Afterward, the search became more focused, looking particularly at works about the environmental aspect of AMR. This narrower search served as the basis for the literature review. Scientific articles were identified using online searchable databases, including PubMed, ScienceDirect, and Scopus. General search terms such as "AMR" and "environment" were employed, and no particular date range was chosen. Such a broad search was necessitated by the limited quantity of relevant articles available as a result of the underexplored nature of this topic. Supplementary gray literature was found with similar methods, as well as Google searches for publications by relevant actors like WHO. Interviewees provided additional resources in the form of scientific or gray literature throughout the research process, which were integrated into both the literature review and the analysis.

Following the literature review, primary data was collected via three formal in-person interviews and three informal Skype interviews. All six were in-depth and semi-structured, and they lasted between 40 minutes and one hour in length. This data collection method was key to effectively addressing the two research objectives because of the many gaps that exist in the literature. The interviews tapped the knowledge and experience of individuals who work on research and policy related to the environmental component of AMR. Each interviewee was asked the same two questions regarding his or her perspectives first on barriers and then on solutions, but unique questions related to the individual's expertise were also posed.

A purposive sampling strategy based upon convenience to the experts was used to ensure that, though the sample size was small, a range of perspectives was still captured. Interviewees included three current or previous high-ranking WHO staffers with country-level and global

experience, a program officer at the South Centre who highlighted unique challenges for developing countries, a PhD student who conducts laboratory research on AMR in the environment, and a senior researcher at the University of Geneva's Global Studies Institute whose specializes in the global governance of AMR and the resilience of One Health systems. In addition, an internal WHO briefing and a presentation on AMR at the WHO headquarters were observed, and a tour was taken of the laboratory where the interviewed PhD student worked.

After the interactive research data had been collected, a critical and evidence-based analysis was conducted using a grounded theory approach. Since its development by Glaser and Strauss in 1967, grounded theory has gained popularity and legitimacy as an effective, inductive framework for the synthesis, analysis, and conceptualization of qualitative data; for this reason, it was determined to be the most appropriate methodological approach for this study. Analysis concentrated on the qualitative data collected via the six interviews. First, transcripts or write-ups were produced for each interview. Data was then sorted based upon its relevance to either the first research objective or the second. Data from the first interview that pertained to the first objective was read line-by-line and potential analytical categories were identified and labeled with emic codes derived from the text itself. As themes emerged, all of the data corresponding to each theme was gathered and compared. The same thematic categories were then used to code the data from each of the other interviews. When additional themes emerged, these were given codes as well. After all of the text had been coded, convergences, divergences, and other thematic links were identified. Additional data — including quantitative data from the Global Database for Antimicrobial Resistance Country Self Assessment, observations, and secondary data from literature — were analyzed for relevance to the themes and utilized to supplement primary findings. Data pertaining to the second objective was analyzed using the same process.

This study adhered to ethical research guidelines. Human Subject Review approval was obtained from SIT Nyon's Internal Review Board prior to data collection or analysis. No children or other vulnerable participants were involved in the study. Contact with interviewees occurred under no or minimal risk circumstances and involved non-sensitive topics. Only with consent were interviews digitally recorded. Permission was obtained for the use of all direct quotes.

Finally, there were some difficulties encountered. The main challenge was the non-responsiveness of potential interviewees to inquiry emails. Also, many initially contacted individuals provided references but did not accept interviews themselves. The second issue was the time constraint. Though the ISP period was a month long, the process of reaching out to experts, scheduling interviews, and collecting and analyzing the data was found to be highly time-intensive, especially because the topic's complexity continued to grow as more information was obtained. There were also some methodological limitations. The main one was the sample size, which, as previously mentioned, was quite small (n=6). Thus, while this study aimed to grasp a range of perspectives, it is not an exhaustive account of all possible barriers or solutions.

3. Literature Review

The central problem that this paper addresses is the neglect of the environmental component of AMR. The burden of this global health threat has gained more attention and generated greater concern since the 2015 adoption of the Global Action Plan on Antimicrobial Resistance (GAP-AMR) at the 68th World Health Assembly, as indicated by the proliferation of literature on this topic in journals like *The Lancet* and *BMC Public Health* after its adoption. The GAP-AMR outlined five objectives: 1) to improve awareness and understanding of AMR; 2) to strengthen knowledge through surveillance and research; 3) to reduce the incidence of infection; 4) to optimize the use of antimicrobial agents; and 5) to develop the economic case for

sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions (WHO, 2015).

The action plan also "underscore[d] the need for an effective 'One Health' approach" (WHO, 2015, p. vii) targeting all three of the major dimensions of AMR: human health, animal health, and the environment (Padiyara, Inoue, & Sprenger, 2018). It acknowledged that "drug-resistant bacteria can circulate in…the environment" (WHO, 2015, p. 2) and stated that in addition to the concern raised by AMR in the human and animal health sectors, the "potential impact of antimicrobials in the environment is also of concern to many" (WHO, 2015, p. 2). However, tangible plans for addressing the environmental aspect of AMR were relatively few. In fact, while the word "human" was utilized 51 times in the document, and "animal" was utilized 63 times, the word "environment" was used just six times. This disparity is inconsistent with the One Health approach espoused by experts like WHO's Human Regional Director for Europe, Dr. Zsuzsanna Jakab, who stated that "human, animal, and environment health are all *equally* [emphasis added] responsible for the correct use of antimicrobials and to avert the threat of antimicrobial resistance" (WHO Regional Office for Europe, 2018, n.p.).

Despite the GAP-AMR's relative weakness on the environmental dimension of AMR, this landmark publication was successful in putting the broader threat of AMR on the world stage and in establishing a global governance framework led by the Tripartite Secretariat. The Tripartite, established in 2012, consisted of WHO, the Food and Agriculture Organization of the United Nations (FAO), and the World Organisation for Animal Health (OIE) (Guerra, 2018). In addition to pushing for global action, the GAP-AMR also urged all WHO Member States to adopt their own national action plans (NAPs) within the next two years.

Further progress proved difficult, however, and more commitment and international collaboration was needed, so global leaders convened for a high-level meeting on AMR at the United Nations General Assembly (UNGA) in New York in September 2016. This was only the fourth time in history that a health topic was discussed at the UNGA. The meeting resulted in the establishment of an ad hoc Interagency Coordination Group (IACG) on AMR (WHO, 2016) as well as a political declaration on AMR. Like the GAP-AMR, however, the Political Declaration of the High-Level Meeting of the UNGA on Antimicrobial Resistance (2016) glossed over the environmental dimension of this issue, stating that the "keys to tackling antimicrobial resistance are: the prevention and control of infections in humans and animals" (UNGA, 2016, p. 3.).

About two and a half years later, the IACG produced a report, "No Time to Wait: Securing the Future from Drug-Resistant Infections" (2019), which was given to the Secretary-General of the United Nations (UN) at the 73rd session of the UNGA in April of 2019. This was the first major work of gray literature to somewhat successfully place the environment on equal footing with human and animal health in relation to the issue of AMR, indicating a shift in the conversation that has the potential to lead to more action on the environmental front. However, the report also reminds its audience that very little had been done as of yet to put such words and intentions into practice (IACG, 2019).

Paralleling the progression of gray literature and global commitments on this issue, scientific literature on the environment and AMR has only just begun to be published with some frequency. For example, since late 2017, the journal *Nature Communications* has published articles on AMR and the environment almost monthly, including a few landmark papers like Karkman, Pärnänen, and Larsson's "Fecal pollution can explain antibiotic resistance gene abundances in anthropogenically impacted environments" (2019), Mahnert et al.'s "Man-made

microbial resistances in built environments" (2019), and Hendriksen et al.'s "Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage" (2019). There is consensus among the findings in these articles that both natural and built environments play a major role in the spread and proliferation of AMR. Each also emphasizes that there is still much to be done in terms of research, surveillance, and action.

Additionally, while the majority of work on this topic has historically been conducted by researchers in Europe and North America, a few different perspectives have begun to emerge. For example, in February 2019, Taneja and Sharma published "Antimicrobial resistance in the environment: The Indian scenario." This development is valuable because of the global nature of the AMR threat. The introduction of new research and opinions from a variety of contexts to the current, rather homogenous, body of literature may encourage innovation and progress.

The lack of attention that has been given to the environmental aspect of AMR and the gaps in gray and scientific literature that remain have generated discussion among a few key individuals in the global health community who are now attempting to shed some light on this problem. One such pioneer, Dr. Sabiha Essack, wrote an article in *The Lancet Planetary Health* in 2018 — "Environment: The neglected component of the One Health triad" — with exactly this purpose. Her article drew heavily upon a monumental work of scientific literature in this field by Larsson et al. (2018), which accumulated knowledge from more than 100 studies published in the twenty-year period between 1998 and 2018 regarding the role of the environment as a transmission route for bacterial pathogens. This paper, which was a product of one of the leading platforms for research and engagement to curb AMR, the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), identified major knowledge gaps associated with the transmission and evolution of resistance in the environment and called upon

"researchers, funding organizations, policymakers and other relevant stakeholders to take the steps needed to fill these knowledge gaps" (Larsson et al., 2018, p. 136). Essack's article, however, went beyond Larsson et al.'s argument, calling attention to gaps not just in research and understanding, but also in strategy, coordination, and national and global action (Essack, 2018).

In conclusion, the environmental dimension of AMR has long been neglected in research and policy, and until very recently, no one has called attention to this issue. A shift is occurring, and scientists, global health governance experts, and policymakers are now beginning to acknowledge it. Still, in order to effectively solve this problem, the barriers that have hindered research and policy related to the environmental aspect of AMR must be identified and analyzed. After establishing an understanding of these factors, then current and future solutions for overcoming those barriers must be similarly identified and analyzed. This is what this paper seeks to do, by gathering expert perspectives, identifying convergences and divergences among them, and linking them to literature and to recent national and global efforts to tackle AMR.

4. Results and Analysis

During data analysis, a number of themes emerged regarding the barriers to research and policy on the environmental aspect of AMR (Objective 1) and the existing or potential solutions for overcoming the neglect of the environment in relation to AMR (Objective 2). These barriers and solutions were relevant at either the global- or country-level, or sometimes both, and are identified as such. In Section 4.1, results related to barriers are organized by thematic category, described, and analyzed. The same is then done in Section 4.2, but for results related to solutions.

4.1 Barriers to Research and Policy on the Environmental Aspect of AMR

The neglect of the environmental dimension of AMR is not surprising given the many barriers that were identified. Barriers ranged from characteristics of the issue, to societal norms

and priorities, to leadership and coordination failures. The following subsections describe and analyze these barriers, which were conveyed by interviewed experts, discovered in literature, and observed at a WHO internal briefing and during an AMR lab visit at the University of Geneva.

4.1.1 Issue complexity and intractability.

One barrier, which was directly identified or alluded to by each interviewee, is the complexity of AMR in the environment and its relative intractability given this complexity. First of all, there is no common definition of what, in relation to AMR, is meant by the 'environment.' The concept was described by Dr. Elizabeth Tayler as "messy" and lacking specificity (personal communication, Nov. 4, 2019). Observations from an internal WHO briefing about their new Tripartite Zoonosis Guide (TZG) — intended to support countries in using a One Health approach to address health challenges at the human-animal-environment interface like AMR — supported this finding. When asked for further explanation of the environmental component of the approach, which had, until that point, been given only a cursory mention, the speaker said that the inclusion of the environment had always been a "sticky part" for the Tripartite and for the broader global health community due to the nebulous nature of the concept and the confusion regarding who or what it includes (personal communication, Nov. 4, 2019).

Without a clear understanding of what it is that should be measured, research cannot occur. This lack of clarity is also not conducive to any sort of case that might be made to policymakers for more funding, attention, or action (D. Wernli, personal communication, Nov. 5, 2019). The fact that "the environment is the most dynamic and consequently the most confounding sector of the One Health triad" (Essack, 2018b, p. e238) is one of the foremost barriers to research and policy related to the environmental dimension of AMR.

4.1.2 Funding, research, and knowledge gaps.

Another barrier, which is linked to the first, is the lack of research and therefore, the lack of evidence, that exists on AMR in the environment. This is another factor that each and every expert touched on in his or her interview. According to Dr. Astrid Wester, the fact that "science cannot actually tell who or what sector is the greater contributor in different settings" is "a major hindrance for action" (personal communication, Nov. 11, 2019). An August 2018 publication by Larsson et al. expressed the same view, finding that research is still urgently needed in a variety of areas related to AMR and the environment.

A number of factors are driving this scarcity of research, but the biggest one is a lack of funding. Resources are limited, and AMR has to compete with other prominent issues in the environment, like climate change, for funding. This was discussed by both Dr. Elizabeth Tayler (personal communication, Nov. 4, 2019) and Dr. Didier Wernli (personal communication, Nov. 5, 2019). As for the funding that has been allocated to AMR research, "most…has been devoted to AMR in hospitals because it's clinical research" (D. Wernli, personal communication, Nov. 5, 2019). This may be changing, as multiple interviewees noted that there appears to be far more research being conducted on the environmental dimension of AMR today than there was in the past. Dhafer Al Salah, who has been researching AMR in the environment since 2014, hypothesized that this increase in attention — and therefore, in research funding — may be due to a rise in deaths and infections caused by drug-resistant pathogens, which, in places like the U.K., where healthcare is publicly funded, is extremely costly for the government (D. Al Salah, personal communication, Nov. 5, 2019). Despite this trend, however, many research gaps remain.

Insufficient research then precludes the implementation of evidence-based policies because, as stated by Dr. Sabiha Essack, "research gaps lead to policy gaps" (personal

communication, Oct. 31, 2019). Even in the human and animal health sectors, where evidence is far more prevalent (E. Tayler, personal communication, Nov. 4, 2019), it has been a fight to bring about change. It can be reasoned, therefore, that policy related to the environmental dimension of AMR — where even foundational knowledge is limited — is far less likely to be developed.

4.1.3 Conflict with existing norms and priorities.

Yet another barrier is that current norms and priorities are not conducive to progress related to the environmental aspect of AMR. Though respect for the environment and awareness of consumption and waste are growing, "we are not there yet" (D. Wernli, personal communication, Nov. 5, 2019) in terms of putting the environment ahead of other interests, like economic development or individual freedom. AMR — and in particular, its environmental dimension — was frequently referred to by interviewees and in the literature as a 'Tragedy of the Commons' issue, in which "individuals are working in their own interest to the detriment of the wider community" (S. Y. Essack, personal communication, Oct. 31, 2019). No one wants to claim ownership for the problem (A. Wester, personal communication, Nov. 11, 2019), and as a result, no one has taken action to solve it.

Another aspect of this barrier, which was identified at the country level, has to do with the different approaches that are taken in regard to potential health threats. Some countries employ the precautionary principle as a guiding framework for their policies. According to this approach, an action must be proved unharmful before it is permitted to occur. In other countries, however, the opposite approach is taken — business as usual continues until it is proved that an action is definitively harmful. Both Dr. Tayler and Dr. Wester, reflecting upon their experiences working at WHO, described how challenging it can be to develop global policies or frameworks when countries are not on the same page regarding how to treat an issue. Because "bacteria don't

need passports" (D. Al Salah, personal communication, Nov. 5, 2019) to cross borders, unilateral actions have major impacts on whether or not this global health threat is effectively addressed. Thus, when countries have different approaches to addressing potential health threats, progress is hindered not just on the environmental aspect of AMR, but also on the issue of AMR in general.

4.1.4 Lack of leadership from environmental actors.

A lack of leadership from environmental actors was another recurrent theme in the interview data and in the literature. "The main interest [in AMR] does not come from environmental constituents…it mainly comes from, I think, people in human health…who start to study the problem in the environment" (D. Wernli, personal communication, Nov. 5, 2019). While both WHO and FAO focus partly on the environment, most of those in leadership positions regarding the AMR threat are not "directly related to the environmental field" (D. Wernli, personal communication, Nov. 5, 2019). This weakness poses a significant barrier to integrating the environmental aspect of AMR into national and global conversations and policies. A prime example of this is the fact that the key governance body on AMR — the Tripartite — lacks environmental representation. Composed of WHO, FAO, and OIE, the Tripartite takes into account the human and animal health sectors, but the absence of an actor with environmental expertise like the United Nations Environment Programme is obvious (UNEP) (S. Y. Essack, personal communication, Oct. 31, 2019). When mentioned in gray or scientific literature on AMR governance, UNEP appears subordinated to the Tripartite or mentioned only briefly in an attempt to cover all of one's bases. For example, on the WHO webpage for the Workplan on AMR it is stated, "WHO, FAO, and OIE have collaborated to develop a Tripartite Workplan…on antimicrobial resistance, with the involvement of UNEP" (WHO, 2019e, n.p.). The draft

document for the plan itself, however, contained no mention of the environment or of UNEP (WHO, FAO, & OIE, 2018a).

This issue appears to have a simple fix (just include UNEP!), but a number of underlying barriers prevent UNEP from taking on a role like those played by the Tripartite members. OIE is institutionally and financially independent from the UN, and WHO and FAO are both UN specialized agencies (A. Wester, personal communication, Nov. 18, 2019). As such, they coordinate their work with the UN but are autonomous organizations. Furthermore, they are funded by both voluntary and assessed contributions (UN, 2019). UNEP, by contrast, is a UN program, financed only by voluntary contributions (UN, 2019). This constraint, in a world in which resources (especially for environment-related projects) are already limited, means that UNEP cannot do it all. They are forced to prioritize the issues that most closely align with their mandate and philosophy, such as climate change. This links back to other barriers like funding gaps and conflict with existing priorities. Finally, it must be noted that despite UNEP's environmental expertise, it does not necessarily have the "answers everybody's been grappling with" (M. Alas, personal communication, Nov. 15, 2019) in terms of AMR in the environment. As a result, "[the environment]'s falling between every chair" (A. Wester, personal communication, Nov. 18, 2019).

4.1.5 Failure to coordinate and collaborate.

Beyond the lack of environmental leadership, there are also other leadership-related barriers — in particular, failures related to coordination and collaboration across sectors, among stakeholders, and between researchers and policymakers. Both Dr. Sabiha Essack and Dr. Elizabeth Tayler described the "silos" in which the three areas of One Health — human health, animal health, and the environment — continue to be studied and targeted in relation to AMR (S.

Y. Essack, personal communication, Oct. 31, 2019) (E. Tayler, personal communication, Nov. 4, 2019). While the human and animal health sectors, through the work of the Tripartite, are attempting to collaborate in order to overcome this barrier, the environmental dimension is still relatively divorced from these efforts.

Part of the reason that the environment continues to be neglected is because there are "so many different players" (S. Y. Essack, personal communication, Oct. 31, 2019) when it comes to the environment. The challenge of coordinating the various stakeholders involved — from environmental ministries to water and sanitation ministries, from hospitals to pharmaceutical companies, and more (S. Y. Essack, personal communication, Oct. 31, 2019) — is a significant barrier at both the global and country levels (E. Tayler, personal communication, Nov. 4, 2019).

The interview conducted with researcher Dhafer Al Salah provided additional insights regarding this barrier. He spoke about what he saw as a lack of correspondence between science and policy, particularly in the area of wastewater treatment (D. Al Salah, personal communication, Nov. 5, 2019). At this point, he said, policies are only focused on live, indicator bacteria, and they fail to acknowledge other factors of significant concern that have been discovered by the scientific community like antibiotic resistant genes (D. Al Salah, personal communication, Nov. 5, 2019). Beyond this research-policy disconnect, it was observed that the interviewee himself was unfamiliar with the concept of One Health and with the AMR research that is currently being conducted in the animal health or human health sectors. All of these failures of coordination and collaboration are major shortcomings that have contributed to the neglect of the environmental dimension of AMR.

4.1.6 Country-level differences.

Differences at the country level — in terms of levels of development, progress on AMR overall, and work that has be done on the environmental dimension in particular — were the final major barrier identified. These differences were made evident in a July 2018 report that charted the progress made in 154 countries on the development and implementation of their NAPs. The report identified major discrepancies, and while it acknowledged that all countries have room for improvement, low-income countries were found to be less successful, in general, than high-income countries (WHO, FAO, & OIE, 2018b). The report also noted a considerable lack of data and action related to the environmental sector. In fact, an analysis of quantitative data from the Global Database for Antimicrobial Resistance Country Self Assessment revealed that — as of survey year 2018-19 — only 94 out of 159 countries (59%) had reported actively involving the environmental sector in the development and implementation of their NAPs. Upon disaggregating the data, it was found that the environment is even more neglected in some regions than others. For example, in the African region, just 6 out of 31, or about 19%, of countries had involved the environmental sector in their plans to combat AMR.

The interviewees confirmed these quantitative findings. They all discussed the barrier of country-level differences, especially between high-income and low- or middle-income countries. In the words of Dr. Didier Wernli: “If you are hungry…if you need to ensure the minimum, you are not going to care for your environment…you live day by day” (personal communication, Nov. 5, 2019). In the vast majority of low- and middle-income countries, which are the focus of Dr. Sabiha Essack’s work on AMR, there is open defecation and water, sanitation, and hygiene infrastructure and practices are not optimal (S. Essack, personal communication, Oct. 31, 2019).

Environmental factors like these produce the “perfect breeding ground for the problem [of AMR] to worsen” (D. Wernli, personal communication, Nov. 5, 2019).

At the time of the study, interviewee Didier Wernli was conducting a JPIAMR-funded research project on the kinds of factors (“determinants”) described above. The aim of the project was to discover the environmental characteristics that make some countries better able to cope with the challenge of AMR than others. As an example, Dr. Wernli proposed two extreme cases: India and Sweden. In India, there is a lot of intensive agriculture, there are weak institutions, the challenges of rapid development and urbanization are compounded by a lack of sanitation infrastructure, and there is widespread use of — as well as easy access to — antibiotics. By contrast, Sweden has far less intensive agriculture, very good institutions and infrastructure, and antibiotics are used in a relatively restrictive manner. For these reasons, Sweden is much better situated than India to tackle the problem of AMR, both in the environment and in general (D. Wernli, personal communication, Nov. 5, 2019). Dr. Wernli also noted that climate differences play a role, a factor brought up by scientific researcher Dhafer Al Salah as well. In his interview, Al Salah explained how AMR severity, particularly in regard to the environmental dimension of AMR, varies widely between warmer and colder climates. In countries with tropical climates, for example, there are much higher rates of uptake of resistance genes in the environment than in Northern European countries (D. Al Salah, personal communication, Nov. 5, 2019; Macfadden, McGough, Fisman, Santillana, & Brownstein, 2018).

These country-level environmental differences are a major hindrance to effective global governance, which at least partially explains the many policy gaps that exist in relation to the environmental dimension of AMR. A 2019 article about AMR and the environment in India conveyed this point well, stating that “among the drivers of AMR, it is the contribution by [the]

environment that varies significantly among different geographical regions of the world and hence estimations and directions laid out by any developed nation (for example England) may not be applicable for the rest of the world" (Taneja & Sharma, 2019, p. 120).

4.2 Solutions for Overcoming the Neglect of the Environment in Relation to AMR

While the sheer number of barriers contributing to the neglect of the environmental aspect of AMR can be overwhelming, many solutions have been or could be used to overcome this issue. The solutions identified in this paper are just some of the many possible actions that could be taken. Further innovation and conversations regarding solutions for problems related to the environmental and other aspects of AMR are necessary and encouraged.

4.2.1 Raising awareness.

One practical and actionable solution, which was suggested by four out of the six interviewees, is to raise awareness about the environmental component of AMR. Knowledge catalyzes behavior change (D. Al Salah, personal communication, Nov. 5, 2019). For example, one interviewee, after beginning to work in this field, stopped taking all antibiotic drugs and said that unless it were absolutely necessary for the maintenance of personal or public health, the interviewee would never take them again. Until countries, industries, and individuals are aware of the role that the environment, and more specifically, the role that their anthropogenic activities — which release antimicrobial residues and antimicrobial resistant bacteria into the environment — plays in the proliferation of AMR, they will be neither willing nor able to effectively craft policies and take actions to reduce their negative impacts. This solution is in line with the first objective put forth in the GAP-AMR: "to improve awareness and understanding of antimicrobial resistance through effective communication, education and training" (WHO, 2015, p. vii).

This solution is something that WHO has been working to implement (E. Tayler, personal communication, Nov. 4, 2019). One example of an awareness-raising campaign that already exists is World Antibiotic Awareness Week (WAAW), which occurred this year (2019) between 18 November and 24 November, during the writing of this paper. The purpose of WAAW is to highlight "best practices among the general public, health workers and policy makers to help stop the further emergence and spread of antibiotic resistance" (WHO, 2019f, n.p.). A weakness of this campaign is that it has generally focused on the human and animal health dimensions of AMR, neglecting the environment. If integrated into future WAAWs, the environmental aspect may gain more traction at the international, national, and local levels.

During the interview conducted at the WHO headquarters in Geneva, Dr. Elizabeth Tayler also described another example of an awareness-raising effort that has recently been undertaken (E. Tayler, personal communication, Nov. 4, 2019). Less than a month before the interview, WHO launched the *Health Workers' Education and Training on Antimicrobial Resistance: Curricula Guide*, a document intended to "[cover] a global gap and [build] further on the AMR competency framework by laying out learning objectives and outcomes as they pertain to the main health worker groups involved in the stewardship of antimicrobials" (WHO, 2019b, n.p.). While this publication focuses on health workers and their practices, it could serve as a model for similar publications targeting environmental actors or industries whose waste streams impact the environment (e.g. pharmaceutical manufacturers, medical laboratories, and hospitals).

Despite these and a few other efforts, global awareness of proper antibiotic usage and of the increasing risks of AMR remains low (WHO, 2019f, n.p.). Awareness of the environmental dimension of this problem remains even lower. Awareness-raising solutions like those mentioned

must be expanded and improved upon at the global level, and they must also be implemented at the national and local levels, in order to have a real impact.

4.2.2 Increased investment and research.

Another solution, brought up by each and every interviewee and in much of the literature, is increased investment and research on the environmental aspect of AMR. The gaps that exist in funding for research stem from many of the barriers previously identified, but the primary one is a lack of funding due to the prioritization of other issues like climate change. These issues draw the majority of the funding that exists for environmental research. To overcome this barrier, Dr. Sabiha Essack recommends emphasizing the connection between AMR and other critical issues that have already gained public attention and interest. For example, climate change has an impact on the infection rates of drug-resistant pathogens (S. Y. Essack, personal communication, Oct. 31, 2019). Highlighting this linkage between AMR and climate change could increase buy-in and commitment, as well as channel more funding toward the study of AMR in the environment.

Additionally, though having more data and a better understanding of AMR in the environment are both important outcomes in themselves (A. Wester, personal communication, Nov. 11, 2019), they are not the only valuable end-goals of increased research. Other beneficial outputs include evidence to inform better policies (D. Al Salah, personal communication, Nov. 5, 2019), alternatives that can be used in place of conventional antibiotics (S. Y. Essack, personal communication, Nov. 1, 2019; M. Alas, personal communication, Nov. 15, 2019), and a better understanding of AMR in the environment, as well as of the flow and interaction between the various elements of AMR (E. Tayler, personal communication, Nov. 4, 2019; D. Wernli, personal communication, Nov. 5, 2019). Each of these outputs will help to overcome the barriers that exist to the inclusion of the environmental aspect of AMR in action plans and other policies.

4.2.3 Increased surveillance and stricter standards.

In addition to increasing awareness and promoting further research, two other solutions supported by the majority of interviewees are increased surveillance of AMR in the environment and stricter standards on anthropogenic activities that produce waste streams contaminated with antimicrobial residues and antimicrobial resistant bacteria. This solution is urgently needed (D. Al Salah, personal communication, Nov. 5, 2019; D. Wernli, personal communication, Nov. 5, 2019) because at this point, there is no concrete guidance for national policymakers and stakeholders on AMR containment in the waste and environment sector (Khurana & Sinha, 2019). This gap in guidance has contributed to lenient or nonexistent waste restrictions and thus to the release of massive quantities of antibiotics, residues, and bacteria into the environment. Illustrating the need for more surveillance and stricter standards, one study in India found that "the levels of ciprofloxacin in surface water around the Indian [drug production] plant exceeded human therapeutic blood plasma concentrations" (Kristiansson et al., 2011, p. 1).

Different countries are at different stages in terms of their surveillance mechanisms and restrictions. In addition to building up country-level monitoring systems, it is important to standardize surveillance because of AMR's potential to spread across borders, especially when it is in the environment (E. Tayler, personal communication, Nov. 4, 2019). The good news is that WHO has launched a collaborative system for doing exactly that: the Global Antimicrobial Resistance Surveillance System (GLASS). Introduced in 2015 and currently concluding its early implementation phase, GLASS aims to strengthen the AMR evidence base (WHO, 2017a). Right now, the system is limited to surveillance of bacterial pathogens in humans (WHO, 2017a), and only 86 countries are enrolled (WHO, 2018b), but there are plans to progressively expand GLASS to include other types of surveillance, including that of AMR in the environment. In

addition, any country can enroll at any stage in the development of its own surveillance system. This stepwise approach encourages the participation of more and more countries over time, as they acquire the resources needed to improve their national surveillance systems (WHO, 2017a).

An additional benefit of increased surveillance of AMR in the environment is that, in the words of interviewee Dhafer Al Salah: “It serves as a warning sign” (personal communication, Nov. 5, 2019). Monitoring environmental AMR enables scientists and policymakers to stay a step ahead of the AMR threat. If this dimension continues to be neglected, however, drug resistant pathogens will only ever be caught once they reach human beings and “it’s already too late” (D. Al Salah, personal communication, Nov. 5, 2019).

Due to the barriers posed by the complex and — at this point — relatively intractable nature of AMR in the environment, this particular solution will not be easy to implement. However, if executed concomitantly with other solutions that provide the investment, data, and awareness needed for this solution to come to fruition, increased surveillance measures for AMR in the environment and stricter environmental standards will lead to more inclusive AMR governance and policy, as well as more timely action after the identification of a drug resistant pathogen in the environment. This could, in turn, save lives.

4.2.4 Coordination, collaboration, and integration of environmental leaders.

Solutions are also needed to address leadership-related barriers, including the lack of leadership from environmental actors and the failure of leading agencies at the global level, as well as at the national level, to coordinate and collaborate. First, in terms of the integration of environmental leaders, “it would be great to have [UNEP] involved because there is this gap in what we do with the environment” in relation to AMR (M. Alas, personal communication, Nov. 15, 2019). While UNEP may not have all of the answers, its addition to the existing Tripartite

would call needed attention to the environmental aspect of AMR. At the time of this study, it appeared that this solution was already beginning to take shape. After the signing of the Tripartite's "Memorandum of Understanding" to step up joint action on AMR on 30 May 2018, a "Tripartite Plus" Workplan was outlined with UNEP apparently "'on board' and a formal relationship…being explored" (Guerra, 2018, p. 3). The source of this information, a WHO document, was the first document observed in this study to have the UNEP logo represented alongside those of the three Tripartite members (Guerra, 2018, p. 1).

In addition to the integration of environmental actors into AMR leadership, coordination and collaboration must be improved among the various sectors and stakeholders involved with AMR. This is true at all levels, and in addition to improving their own partnerships, international agencies should guide and facilitate countries in coordinating national-level efforts. According to a policy brief from the South Centre, countries need to be supported in "set[ting] up national inter-ministerial committees…[to] help break the silos" (Alas & Tellez, 2018, p. 2). These committees should involve the agricultural and health sectors, as well as the environmental ministry. AMR, and the environmental aspect of it in particular, is "really a whole of community issue" (A. Wester, personal communication, Nov. 11, 2019). As stated by Dr. Sabiha Essack, it is "everybody's responsibility" (personal communication, Oct. 31, 2019), and therefore "everybody needs to change" (E. Tayler, personal communication, Nov. 4, 2019). This means that efforts that fail to include all relevant agencies and actors — including environmental experts — are insufficient to address the health threat of AMR. Future policy and action must stem from truly collaborative efforts across the human-animal-environment interface.

4.2.5 Support for developing countries.

While it can be said that most, if not all, countries have room for improvement in terms of addressing AMR in the environment, many developing countries in particular lag far behind due to a lack of resources, guidance, and support. Mirza Alas from the South Centre provided insight into this topic, describing how while some developing nations have made efforts to integrate the environmental sector in their response to AMR (such as India in their NAP and more recently Malaysia), others are struggling to address AMR at all — let alone the environmental aspect of the issue (M. Alas, personal communication, Nov. 15, 2019). To solve this problem, the global community should invest in developing nations' technical capacities, human resources, and infrastructure.

However, as pointed out by Dr. Astrid Wester, it is important that support given to developing nations is both desired by recipient countries and sustainable (personal communication, Nov. 11, 2019). This means that innovative financial solutions, the specifics of which were beyond the scope of this paper, are needed to prevent dependence on donor government money. Furthermore, while the guidance that the Tripartite currently provides for the development and implementation of NAPs is a good starting point, far more still needs to be done to support countries in creating structures to combat AMR that work across all relevant sectors, including the environment (A. Wester, personal communication, Nov. 11, 2019). Increasing regional leadership on this issue is one way that this goal might be accomplished, because it would decrease the range of levels of development, types of climate, and other factors that vary from country to country, enabling more targeted assistance.

4.2.6 Advancing the One Health approach.

Yet another solution — the only one that was truly contested among the interviewees — was the continued advancement of the One Health approach as the guiding framework for addressing the threat of AMR. Most of the interviewees expressed the belief that this would encourage more attention to be paid to the environmental dimension of AMR over time. For example, Dr. Didier Wernli described the introduction of One Health as a framing strategy to be one of the few — if not the only — positive shifts that he had seen to date in terms of putting an end to the neglect of this third dimension of AMR (D. Wernli, personal communication, Nov. 5, 2019). Qualifying this statement, he also acknowledged that it is only an approach, and that while the discourse may have finally arrived at the point at which this neglect is being discussed, "discourse doesn't mean action" (D. Wernli, personal communication, Nov. 5, 2019). It is, however, in his opinion — and in the opinions of most of the other interviewees — a good first step (D. Wernli, personal communication, Nov. 5, 2019).

While the general consensus was that the One Health approach is the best solution that exists — at least at this point — for tackling AMR and for ensuring that the neglected environmental aspect of this issue is finally addressed, one interviewee had a different perspective. Dr. Astrid Wester felt that while this approach effectively frames *what* needs to be accomplished, *how* to do it lies "far beyond the One Health sphere" (A. Wester, personal communication, Nov. 11, 2019). The One Health approach, she stated, covers "only the scientific or biological side of things" (A. Wester, personal communication, Nov. 11, 2019), and AMR in the environment is much more complicated than that. There are many social, economic, and structural issues involved, and according to Dr. Wester, failure to address these fundamental, development-related issues will lead to the continued neglect of the environmental dimension of

AMR and limited progress on this global health threat overall (personal communication, Nov. 11, 2019). From this perspective, the One Health approach might be a decent starting point in that it encourages a holistic way of thinking about this issue, but it is not a solution. It will not, by itself, drive progress on the environmental aspect of AMR. To accomplish such progress, solutions must go beyond the One Health framework; they must consider the various other development-related factors that, because of their impact on the environment, also impact AMR.

4.2.7 Environment as a symptom: upstream solutions.

The final "solution" identified in this study is neither a singular action item nor one specific goal to pursue; rather, it is an entirely different perspective on AMR in the environment — accompanied by its own list of solutions. This perspective views the environment more "as a symptom or manifestation of the problem [of AMR] than the cause…for that…it should be addressed more upstream" (D. Wernli, personal communication, Nov. 5, 2019). These "upstream" solutions are manifold, and different suggestions were put forth by different interviewees. Dr. Didier Wernli, for example, discussed preventative efforts like antimicrobial stewardship in the other two sectors of the One Health triad — human and animal health — because he was "not sure that we can address [AMR] in the environment, except maybe some settings like a sewage plant" (D. Wernli, personal communication, Nov. 5, 2019). "Ultimately," he said, "I don't think the solution will come from the environment" (D. Wernli, personal communication, Nov. 5, 2019).

Dr. Astrid Wester shared this perspective, relating it to her belief that solutions for AMR in the environment must go beyond the One Health approach entirely. According to Dr. Wester, the kinds of upstream solutions that are needed will target more fundamental issues of development such as low resources, poor infrastructure, high levels of inequality, and political

instability or corruption (A. Wester, personal communication, Nov. 11, 2019). She stated, "I strongly believe that development is the answer, the most important answer to how to fight AMR" (A. Wester, personal communication, Nov. 11, 2019). Linking this issue to the SDGs, Dr. Wester's concerns converged with those in the literature (Lomazzi et al., 2019) regarding the way that AMR, as a development issue, threatens the achievement of the SDGs. However, she also brought up a new point. This is not a one-way relationship; it is cyclical. Without the implementation of development-related solutions that provide things like "access to clean water for drinking, cleaning and personal hygiene, and access to safely managed sanitation" (A. Wester, personal communication, Nov. 18, 2019), the issue of AMR in the environment cannot be addressed. This is because, as described Dr. Sabiha Essack, improper use of antibiotics is a "Band-Aid" for various other development-related problems that allow resistance to be transmitted within and between environments (personal communication, Oct. 31, 2019). Therefore, the solutions that will overcome the neglect of the environment in relation to AMR are more upstream solutions that aim to improve infrastructure and development.

5. Conclusion

The purpose of this study was to explore the neglect of the environment in relation to AMR and to add nuance to the emerging discussion on this issue. The two-part research question "Why has the environmental aspect of AMR been neglected and what can be done to prevent this neglect from occurring in the future?" was posed, and from this question, two specific research objectives were derived. The first was to identify and analyze the main barriers that have hindered research and policy developments related to the environmental aspect of AMR, and the second was to identify and analyze existing and potential solutions to overcome these barriers.

After an extensive review of gray and scientific literature, data collection began. Three formal in-person and three informal Skype interviews with experts were conducted, observations were recorded at an internal briefing at WHO, as well as at a talk on AMR, and quantitative data was obtained from the Global Database for Antimicrobial Resistance Country Self Assessment. All of this data was then analyzed using a grounded theory approach. Emergent themes pertaining to each of the two research objectives were identified and then evaluated, searching for convergences, divergences, and other linkages.

While it was found that there are many barriers to research, policy, and action on the environmental dimension of AMR, the research also indicated that there are just as many, if not more, existing or potential solutions that have begun to or could be employed in the future to overcome the neglect of the environment in relation to this global health threat. Some of these solutions directly target AMR in the environment, while others focus more upstream and aim to tackle root causes related to a lack of sustainable development and infrastructure. Overall, it was concluded that despite the fact that things are beginning to change, far more still needs to be done. The problem has been identified and a conversation about the neglect of the environmental component of AMR has been initiated. This study contributed to the discussion by identifying and providing an analysis of some of the key barriers that are driving this problem, and well as some of the existing and potential solutions that could be used to overcome it. Future steps should include exploring, testing, and implementing the solutions identified in this paper and developing additional solutions as needed. More research and surveillance are needed to improve understanding and awareness regarding AMR in the environment. Accomplishing these things, however, will require increased funding and commitment from national and global leaders.

Policy reform is recommended to enhance coordination and collaboration among the many actors involved in AMR in the environment. Moreover, the input of those with environmental expertise should be included in the development and implementation of all future national and global plans to combat AMR. Additional policy recommendations include increasing financial and technical support for developing countries, so that they are better able to address AMR in the environment. While the One Health approach should continue to be advanced, overcoming the neglect of AMR in the environment will require policymakers to go beyond this approach. They will have to also find ways to address the underlying causes of this issue, which are rooted in poor infrastructure and low levels of development.

Finally, though it was beyond the scope of this study, it is recommended that the potential application of the global governance framework for climate change to the issue of AMR in the environment be explored as well. This was a concept that was touched upon in the literature and in two of the six interviews and appeared to have great promise. However, the time constraint prevented sufficient exploration or analysis, and therefore no conclusions could be drawn. It is recommended that this concept is studied in greater depth in the future, in consultation with not just experts on AMR in the environment, but also experts on climate change governance.

6. Abbreviations

AMR	Antimicrobial Resistance
IACG	Interagency Coordination Group
FAO	Food and Agriculture Organization
GAP-AMR	Global Action Plan on Antimicrobial Resistance
GLASS	Global Antimicrobial Resistance Surveillance System
NAP	National Action Plan
OIE	World Organisation for Animal Health
SDGs	Sustainable Development Goals
TZG	Tripartite Zoonoses Guide
UN	United Nations
UNEP	United Nations Environment Programme
UNGA	United Nations General Assembly
WAAW	World Antibiotic Awareness Week
WASH	Water, Sanitation, and Hygiene
WHO	World Health Organization

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